CERTIFICATE OF MAILING
37 C.F.R. 1.8

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10/29/03
Date

Mark B. Wilson

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Conrad

Serial No.: 09/854,412

Filed: May 11, 2001

For: HIGH EFFICIENCY mRNA ISOLATION METHODS AND COMPOSITIONS

Group Art Unit: 1636

Examiner: Katcheves, Konstantina

Atty. Dkt. No.: AMBI:073US

CORRECTED DECLARATION OF RICHARD C. CONRAD, PH.D, UNDER 37 C.F.R. §1.132

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Richard C. Conrad, Ph.D., declare the following:

1. I am an inventor of the above-referenced patent application. I am a Senior Scientist at Ambion, Inc. and have worked there for three years (since March, 2000). I have a Ph.D. in Molecular Biology, which I received in 1987 from The University of Wisconsin at Madison. I was a postdoctoral fellow at Indiana University for nine years and at Eli Lily and Company for two and a half years, as well as Facility Manager at Indiana University for two years. I have worked in the field of molecular biology, including nucleic isolation

techniques for approximately twenty-five years. My *curriculum vitae* is attached as Exhibit 1.

2. I understand that the claims in this application have been rejected as not novel or obvious over U.S. Patent No. 5,759,777 issued in the name of Kearney *et al.* ("Kearney patent").

3. I have reviewed the Kearney patent and believe it does not disclose or teach my invention.

4. My invention is based on my discovery that some problems with mRNA isolation stems from rRNA carryover that is based not on rRNA interactions with the targeting molecule, such as oligo-dT, but on rRNA interactions with mRNA. *See* specification at page 4, lines 25-28; Examples 1 and 2.

5. The use of TEAC and TMAC minimizes differences in bond strength between A:T and G:C basepairs, as G:C basepairing is known to be stronger than A:T basepairing. Isolation of mRNA based on A:T basepairing is affected in the presence of TEAC or TMAC. Stretches of A:T basepairing between mRNA and a poly(T) or poly(U) nucleic acid can be positively exploited at the expense of G:C and A:T basepairing between mRNA and rRNA to reduce the carryover of rRNA. *See* specification at page 4, line 28 to page 5, line 7. Furthermore, I believe the TEAC and TMAC reduce basepairing between the rRNA and mRNA, as well as rRNA and a poly(T) or poly(U) nucleic acid that might be employed to hybridize with the mRNA.

6. Based on my knowledge of the field, I believe that if one did not know or appreciate that rRNA carryover as a contaminant in a mRNA sample can be attributed to hybridization between rRNA and mRNA or between rRNA and a poly(T) or poly(U) nucleic acid, then

that person would not consider the use of TEAC or TMAC in an mRNA isolation procedure.

7. I hereby declare that all statements made of my own knowledge are true and all statements made on information are believed to be true and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

Oct 29, 2003
Date

Richard C. Conrad, Ph.D.